

Technical Department Phibro Animal Health Corporation

HEALTHY ANIMALS. HEALTHY FOOD. HEALTHY WORLD."







# Major points

for the implementation of an anticoccidial program.

Technical Department Phibro Animal Health Corporation

While not a novel disease – first pathogenic coccidia in poultry have been described by Railliet and Lucet in 1891 (130 years ago) coccidiosis is still one of the most economically important diseases in modern broiler industry being responsible for annual losses of more than \$3 billion (Noack et al 2019; Kadykalo et all 2017).

concern.

Coccidia are omnipresent and very robust in the environment, therefore, cannot be eradicated. For this reason, the use of coccidiostats (in-feed anticoccidials) for the control of coccidiosis is deemed essential (EU COMMISSION 2008).

program.

Coccidiosis in poultry is caused by obligate intracellular protozoa (unicellular eukaryotes) from the genus *Eimeria*. There are seven species pathogenic in domestic fowl. Four of them E. acervulina, E. maxima, E. tenella and E. mitis have economic importance in broilers. E. necatrix and E. brunetti affect birds over six weeks of age and are pathogenic primarily for rearing breeders and layers as well as slow growing broilers, while *E. praecox* is less or not pathogenic.

*Eimeria* invade intestinal epithelial cells, destroying them leading to intestinal inflammation, diarrhea (sometimes hemorrhagic), poor absorption of nutrients (increased FCR and reduced weight gain), and sometimes even mortality. Eimeria are the most common triggering factors of secondary intestinal disorders such as Necrotic Enteritis and Dysbacteriosis which have further devastating effects in poultry. Finally, Eimeria facilitate the colonization of the organism by pathogens such as Salmonella sp., which are major food safety

To help build the best anticoccidial program for the given conditions, we developed this practical e-book, which brings in, the main points to be considered for an efficient implementation of an anticoccidial

# tools

# Knowing the anticoccidial

# Identify the most effective molecules for the existing problem

One of the most important points within the control and prevention measures for coccidiosis in broiler chickens is selecting the right anticoccidial product and correctly implementing into the operation.

At Phibro we believe this decision is complex. While on the surface it might appear the only factors to consider are: the molecule to be used, the best price and then mixing it in the birds' feed throughout. The evaluation of all factors need to be considered to provide a high efficiency program for your poultry production.

There are two major aspects to review – safety and resistance.

# Safety

Anticoccidial drugs might cause adverse effects in target species when overdosed. Some of the anticoccidials (e.g. ionophores, halofuginone, nicarbazin) when accidentally fed to other species might cause detrimental effects and even mortality. Withdrawal periods for each drug should be followed to ensure drug residues are below safe levels in end consumer product.

# **Resistance**

Resistance is the ability of a parasite strain to multiply or to survive in the presence of concentrations of a drug that normally destroy parasites of the same species or prevent their multiplication (Chapman, 1997).

efficacy of the product declines.

Resistance development initiates with a genetic shift (single or multiple mutations) allowing the parasite to escape or resist the drug MoA (Mode of Action). Spreads in the parasite population enforced by the selection pressure of using the given product (the longer the drug is used the more resistance is enforced among the field *Eimeria* population - Peek and Landman, 2011)

Resistance development is an inevitable consequence of the use of any product. It could be partial or even complete and should be distinguished from the subtle differences in sensitivity of different native strains of *Eimeria* species to different products.

Resistance is reversible when the selection pressure is removed (Chapman, 1997).

# Resistance development is a natural selection process. After a period of use of any given product the *Eimeria* population in the field develops resistance thus, the

# **Ionophore anticoccidials**

Since their first introduction on the market in the 1970s, ionophores have been the backbone of anticoccidial programs worldwide.

They are produced by fermentation and share a similar mode of action – affect cell membrane permeability and facilitate the ion transport across, thus impair the normal cell metabolism. They have dose dependent effect against extracellular forms of the parasite – sporozoites and merozoites.

lonophores don't completely block the development of the parasite, allowing also sensitive individuals to proliferate, which reduces the selection pressure, therefore resistance is built slowly and allows for immunity development.

Based on their chemical structure and properties, ionophores are divided into 3 groups – monovalent, divalent and glycosides (Peek and Landman, 2011; Noack et al., 2019). Due to the shared mode of action there is certain cross resistance between different ionophores, though there are differences in sensitivity between the different classes of ionophores e.g. a given *Eimeria* isolate could develop resistance towards monovalent ionophores (monensin, salinomycin and narasin), but still be sensitive towards a glycoside ionophore or the other way around (Bedrnik et al., 1989).

Indirect evidence of cross resistance is the resistance against narasin, described even before its introduction to the market, explained by resistance developed after use of monensin and salinomycin (other monovalent ionophores). (Chapman, 1997).

lonophores exert the same effect over the host cell membranes, thus have low safety margin 10-20%.

lonophores registered for use in broiler feed are listed in the table to the right, as well as doses and chemical structure.

| Monesin*             |
|----------------------|
| Salinomycin*         |
| Narasin              |
| Divalent ionophores  |
| Lasalocid            |
| Glycoside ionophores |
| Maduramicin*         |
| Semduramicin         |

Monovalent ionopho

\* Several su

| res | Dose range                          | Chemical structure  |
|-----|-------------------------------------|---|
|     | 100-120 ppm*                        | $HO \qquad CH_3 \qquad H_3C \qquad H_$                          |
|     | 50-70 ppm*                          | HO $(H_3 CH_3 CH_3 CH_3 CH_3 CH_3 CH_3 CH_3 C$  |
|     | 60-70 ppm                           | $HO \begin{pmatrix} H_3C \\ 0 \\ H \\ H \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ H \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ H \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} H_3C \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ 0 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ CH_3 \\ CH_3 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ CH_3 \\ CH_3 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ CH_3 \\ CH_3 \\ CH_3 \\ CH_3 \end{pmatrix} \begin{pmatrix} CH_3 \\ CH_3 \\$ |
|     | Dose range                          | Chemical structure  |
|     | 75-125 ppm                          | HO =   |
|     |                                     |   |
| 6   | Dose range                          | Chemical structure  |
| S   | Dose range<br>5-6 ppm*              | $H_{3}C$ $Chemical structure$ $H_{3}C \xrightarrow{(H_{3}) \to (H_{3}) \to (H_{3$   |
| 5   | Dose range<br>5-6 ppm*<br>20-25 ppm | $H_{3}C \qquad Hono H = H_{3}C \qquad H$  |

| Chemical or synthetic   | Dose range   | Chemical structure   |  |  |
|---|--------------|--|--|--|
| Nicarbazin*   | 100-120 ppm* | $\begin{array}{c} NO_2 \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$ |  |  |
| Zoalene (DOT)*  | 40-125 ppm*  | O <sub>2</sub> N NH <sub>2</sub><br>NO <sub>2</sub> CH <sub>3</sub>              |  |  |
| Clopidol*   | 125 ppm*     | H <sub>3</sub> C N CH <sub>3</sub><br>CI CI CI<br>OH                             |  |  |
| Decoquinate*  | 20-40 ppm*   | $H_3C$ $O$ $N$ $O$ $CH_3$<br>$H_3C$ $O$ $OH$ $O$ $OH$ $O$                        |  |  |
| Robenidine*   | 30-36 ppm*   |  |  |  |
| Holofuginone*   | 2-3 ppm*     | Br<br>Cl<br>N<br>N<br>H<br>H   |  |  |
| Diclazuril*   | 1 ppm*       |  |  |  |
| * Several suppliers. Always consult the label for approved dosage / supplier. |              |  |  |  |

## Chemically synthetized anticoccidials (Synthetics or Chemicals)

Chemically synthesized anticoccidials were launched commercially in the 1940's. Since then many new compounds have been introduced.

The main and important chemical anticoccidials (listed below) currently used are representatives of different chemical classes with different mode of actions (Peek and Landman, 2011; Kadykalo et all 2017). For this reason, they should not be generalized but reviewed separately.

Different chemicals develop resistance at a different pace – from very rapid (diclazuril and decoquinate); to rapid (robenidine and clopidol) to slow (nicarbazin and zoalene) (Chapman, 1997).

Due to the very different chemical structure and mode of action of the currently available chemical anticoccidials, there is no crossresistance among them. The only exception is diclazuril which has cross-resistance with the inwater treatment toltrazuril (Chapman, 1997).

# **Synergistic combinations**

lonophores and nicarbazin are the most widely used anticoccidial molecules due to their effectiveness against the major *Eimeria* species in domestic poultry *Gallus gallus*, but also their ability to develop resistance slowly and allow for immunity development. In this respect they are perceived as reliable because the risk of a sudden outbreak is lower.

Unfortunately, both ionophores and nicarbazin have narrow safety margins. In addition, nicarbazin increases heat production and increases sensitivity to heat stress (Fowler, 1995).

In order to reduce their effective dose, synergistic combinations of different ionophores with nicarbazin have been developed. This allows for effective coccidiosis control with a lower risk of side effects of the drugs.



# Combo drug Narasin + Nicarbazin Monensin + Nicarbazin Salinomycin + Nicarbazin Maduramicin + Nicarbazin Semduramicin + Nicarbazin

|   | Dose range               | Product Name |  |
|---|--------------------------|--------------|--|
|   | 40-50 ppm +<br>40-50 ppm | Maxiban      |  |
|   | 40-50 ppm +<br>40-50 ppm | Monimax      |  |
|   | 50 ppm +<br>50 ppm       | Salinocarb   |  |
|   | 3.75 ppm +<br>40 ppm     | Gromax       |  |
|   | 15-18 ppm +<br>40-48 ppm | Aviax® Plus  |  |
| *Always consult the label for approved dosage / supplier. |                          |              |  |

# Knowing the infection pressure

# Knowing the prevalence of the problem

A good anticoccidial program reflects the infection pressure on the field and the specifics of the production system. A good coccidiosis infection pressure monitoring program collects data and information to assess prevalence and give feedback. This gives the producer the tools to make decisions on product, dose and duration of use, adjustments and investigations.



# What is coccidiosis monitoring in broilers?

It is a regular and routine assessment of subclinical coccidiosis incidence and pressure in the operation.

It is based on macroscopic and microscopic scoring of intestinal lesions produced by the most economically important *Eimeria* species in broilers – *E. acervulina*, *E. maxima* and *E. tenella*.

The main objective is to gather information and be proactive, taking corrective actions and measures, and planning the coccidiosis management program in view of the analysis of the data collected.

The coccidiosis monitoring data should be interpreted with the overall intestinal health status, performance and overall health of the flocks.

# An adequate sanitary monitoring program should basically cover the following points:

**01.** Training of the team that will perform the monitoring (lesion scoring, scrapings, etc.).

**02.** Definition of frequency, monitoring sampling and items to be monitored.

**03.** Management of health monitoring data.

Let's see each one.

# **01. Training of the Team**



Consistency determines the success of a monitoring system. Training is necessary and decisive for the team to enhance the knowledge and skills in detecting macroscopic pathological changes, but another very important point, even before training, is the choice of people/coordinators responsible for carrying out and managing the health monitoring program.

Without the correct understanding of the purpose (of the monitoring management), of the commitment to collect data in a correct and systematic way, the data will often not reflect the field situation. Doing it correctly and with good management is fundamental.

It is very important to establish a frequent training routine for the teams in charge of monitoring. Verifying the performance of the team and the retention of the training offered is fundamental, but often overlooked. Are those responsible for monitoring (execution and management) able to carry out the monitoring tasks? Regular training and verification sessions with industry experts or vendors are useful to maintain consistency of the scoring teams.





# 02. Monitoring: scope, frequency, sampling

Coccidiosis monitoring is part of the integral health monitoring system of the operation. The most objective field evaluation system is based on macroscopic intestinal lesion scoring and microscopical identification of oocysts in the intestinal mucosa of scored birds.

The most economically important *Eimeria* species in broilers have a different predilection place and produce distinct characteristic lesions (e.g. *E. acervulina* produces whitestriped kind of lesions on the mucosal side of the duodenum; *E. maxima* produces characteristic pin point hemorrhagic lesions visible from the serosal side of the jejunum and *E. tenella* produces characteristic hemorrhage in the ceca).

To assess the severity of subclinical coccidiosis a reliable, a 0 through 4 scoring system has been developed (Johnson and Reid, 1970). The downside of the system is that especially mild lesions (1-2) of *E. maxima*, might be under or

over estimated. For this reason, it is good to confirm them with microscopical scoring – identification of *E. maxima* oocysts in scrapings from the intestinal mucosa of the scored birds.

To assess the coccidiosis incidence and infection pressure within a given operation (integration or all farms supplied by a given feed mill) regular necropsy sessions (often called posting or lesion scoring sessions) should be carried out. They should be planned on operation level including flocks from different farms representative for the integration. Each session should include at least ten different flocks representing different ages ranging from 18 to 38 days of age. Typically, 5 average-looking birds per flock, randomly-picked at different places of the house are selected. Only average, healthy birds should be selected (not clinically diseased or dead birds). Scoring should take place immediately after birds are euthanized. The postmortem process might destroy some lesions, therefore scoring should happen right after euthanizing the birds.

# Tips:

- Monthly or weekly
- Same protocol, Every time
- Different farms at different ages (18 to 38 days of age)
- At least ten different flocks per session (e.g. 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38 days of age)
- Five healthy birds/flock (No mortality or clinically-ill birds)
- Systematic approach combining macroscopic lesion scoring and scrapings
- Take your time, don't rush the job
- Need good light and a microscope



# E. acervulina (affects mostly the duodenum)

### Lesion score +1

Scattered white plaque-like lesions containing developing oocysts confined to the duodenum.

These lesions are elongated with the longer axis transversely oriented on the intestinal walls like the rungs of a ladder.

They may be seen from either the serosal or mucosal intestinal surfaces.

They may range up to a maximum of 5 lesions per square centimeter.

There can be some loss of pigmentation and some loss of performance.



## Lesion score +2

Lesions are much closer together, but not coalescent. They may extend as far posterior as 20 cm below the duodenum in 3-week-old birds. The intestinal walls show no thickening. Digestive tract contents are normal. There can be some loss of pigmentation and some loss of performance.





*E. acervulina* (affects mostly the duodenum)

### Lesion score +3

Lesions are numerous enough to cause coalescence in the lesion size, giving the intestine a coated appearance.

The intestinal wall is thickened, and the contents are watery.

Lesions may extend as far posterior as the yolk sac diverticulum.

There can be some loss of pigmentation and loss of performance is well known.

Diarrhea



#### Lesion score +3

## Lesion score +4

The mucosal wall is greyish with individual lesions completely coalescent.

Congestion – may be confined to small petechiae or in extremely heavy infestation, the entire mucosa might be bright red in color.

Individual lesions may be indistinguishable in the upper intestine, typical ladder-like lesions appear in the jejunum.

The intestinal wall is very much thickened, and intestine is filled with a creamy exudate, bearing a large number of oocysts.

Watery diarrhea.





# E. maxima

(affects mostly the Jejuno-illeum)

## Lesion score +1

The serosal surface may be speckled with numerous red petechiae, and the intestine may be filled with orange mucus.

There is little or no ballooning of the intestine.

The intestinal wall is not thickened.

There could be some weight and pigmentation loss.



# Lesion score +2

Serosal surface may be speckled with numerous red petechiae.

Intestine might be filled with orange mucous. Little or no ballooning of the intestine. Thickening of the intestinal wall. Performance and pigmentation loss.





# E. maxima

(affects mostly the Jejuno-illeum)

# Lesion Score +3

Serosal surface may be speckled with numerous red petechiae.

Intestine might be filled with orange mucous.

Little or no ballooning of the intestine.

Thickening of the intestinal wall.

Performance and pigmentation loss.



# Lesion Score +4

Intestinal wall may be ballooned for most of its length. Contains numerous blood clots and digested red blood cells giving a characteristic color and putrid odor. The wall is greatly thickened. Significant adverse effect on performance and pigmentation.

Diarrhea (sometimes bloody with digested blood), dehydration and mortality.





# E. tenella

(affects mostly the ceca)

# Lesion Score +1

Very few scattered petechiae on the caecal wall

No thickening of the caecal wall.

Normal caecal contents are present.



# Lesion Score +2

Lesions more numerous, with noticeable blood in the caecal contents.

The caecal wall is somewhat thickened.

Normal caecal contents are present.





# E. tenella (affects mostly the ceca)

# Lesion Score +3

Large amounts of blood or caecal cores are present.

Caecal walls are greatly thickened.

Little, if any, fecal contents are present in the caeca.



## Lesion Score +4

Cecal wall greatly distended with blood or large caseous cores. Fecal debris lacking or included in the cores.

Bloody diarrhea (non digested blood) and mortality.



# **Microscopical examination of deep intestinal scrapings**







**No Oocysts** 



Macroscopic lesion scoring is the most reliable tool for estimating the infection pressure and the efficacy of the cocci control program on the field, but to maximize its value, we need to address some limitations namely the *E.maxima* scoring. This species produces characteristic lesions, but they could be overlooked or misdiagnosed especially in mild case 1+ or 2+. To cope with these limitations in the modified system we apply microscopy of deep mucosal scrapings.

It could be a standard part of the scoring protocol; thus we take deep scrapings from 3 standard points (beginning, middle and end of the jejunum) and we introduce an additional score called *E. maxima* micro. We examine the slide under the microscope at 100x magnification and giving a 0 grade when there are no oocysts, +1 when there are less than 10 per visual field; +2 for 10 to 20; +3 for 20 to 40 and +4 for more than 40 per visual filed.

Alternatively we can use scrapings only for confirmation of the macroscopic score especially +1, so we take deep mucosal scraping when we see any sign indicative for *E.maxima* infection (even a single serosal pinpoint petechia, ballooning of the intestine, thickening of the mucosa or orange mucous). We examine the slide under the microscope, and we confirm and record the macroscopic score if we find any *E.maxima* oocyst.

How do we take deep intestinal scrapings? After careful examination of the serosal side, we incise the intestine, examine the intestinal content and the mucosa, then we clean carefully all the intestinal content and with the corner of the coverslip or the tip of the scissors we make a deep scratch of the mucosa. After that we place the material on the microscope slide, cover it with the cover slip and press so we have thin enough specimen for examination. If we have intestinal content or the specimen is too thick it makes examination more difficult and increases the risk of missing oocysts.

#### Mild Infection



#### **Heavier Infection**







# 03. Coccidiosis monitoring data management and interpretation

Lesion scoring should not be interpreted on a bird or a flock base, but rather on integration level. It gives data that should be compared with previous sessions to determine the infection pressure trend. It is also useful to benchmark with other integrations producing under similar conditions.

Different *Eimeria* species have different impact on performance with *E. maxima* being most detrimental for BWG (body weight gain), FCR (feed conversion rate) and absorption of nutrients and *E. tenella* having the lowest impact (Conway 1997).











# Build the most effective program for your specific conditions.

# **ROTATION**

# **Avoid resistance development and cross-resistance**



In order to maximize the effect of the anticoccidial program and achieve its best performance one should mitigate the risk of resistance development. In this respect the duration of exposure of the *Eimeria* population to a given drug should be minimized (Peek and Landman 2011). In order to achieve this a rotation program should be established. **Rotation** - changing the anticoccidial tools to one of the **other classes** after a few cycles.

Optional

Full (straight) program - same anticoccidial from day one to withdrawal (starter/grower/finisher)

Shuttle program - one anticoccidial in the starter/grower and another anticoccidial in the grower/finisher

|    |     | Opti | onal |
|----|-----|------|------|
| 0d | 21d | 37d  | 42d  |

Vaccination could be a part of the rotation program and helps to restore sensitivity of field *Eimeria* to different anticoccidial drugs (Peek and Landman, 2011).

- Stand-alone
- Bio-shuttle vaccination followed by a low dose of an ionophore to alleviate the downsides of the vaccine
- Bio-Phyto shuttle vaccination followed by phytogenic product which alleviates the downsides of the vaccine

Rotations have helped prolong the effective life of anticoccidials in the face of constant

selection for drug resistance (Chapman, 2014)



Using drugs from the same class and same mode of action one after another increases the risk of resistance being developed toward the class.

Rotate between products from different classes to avoid cross-resistance and provide restoration of sensitivity.







lasalocid semduramicin

livalent glycoside

# Don't use any product for too long

The safe duration of use depends on the pace of resistance development inherent for each drug

- lonophores in full/shuttle up to 4-6 months
- Nicarbazin combos in shuttle up to 6 months
- Other chemicals in full up to 2-3 months.
- Other chemicals in shuttle up to 3-4 months



Give as long a resting period as possible for each class lonophores at least 6 months Chemicals at least 12 months

> \*to be able to give the whole class of a resting period one should combine in shuttle programs nicarbazin-ionophore combos with ionophores from the same class (e.g. Aviax Plus/Aviax or Maxiban/Salinomycin or Maxiban/Narasin)

#### Do not use a certain product for too long.



To avoid loss of performance or management issues the side effects of some of the anticoccidials should be considered.

Safety margin - some anticoccidials have rather narrow safety margins (all ionophores, halofuginone, nicarbazin) – for this reason they should be carefully dosed, properly mixed and special attention should be paid to avoid de-mixing (segregation) of the feed in case of mash feed, poor pellet quality etc.

**The dose** of the above products should be reflecting the infection pressure – low infection pressure low end dose, moderate to high infection pressure mid range dose and only in very high infection pressure high end dose.

Nicarbazin increases the heat production and sensitivity towards heat stress from 40ppm (Fowler 1995) – limit the use of nicarbazin/nicarbazin containing products to the first 21/28d of age and avoid use in heat stress risk periods if the poultry house temperature cannot be maintained below 21°C.

Lasalocid increases water intake and respectively water excretion – limit the use during cold and humid periods of the year when excessive humidity cannot be evacuated from the house.

Monensin limits the feed and water intake, especially under high temperature conditions - avoid using it during summer.

# **Consider side effects of different anticocidials**





# Basic and important points in a well-designed anticoccidial program:

# 1.

Do not use any given product for too long

Consider the rate of resistance development for different products.

- Ionophores in full program/ nicarbazin-ionophore shuttles or combo/ - 4 to 6 months.
- Other chemicals in full 2 to 3 months of in shuttle 3 to 4 months.

# 2.

Rotate between different classes (not between products or molecules from same class).

# 3.

After each period of use give a sufficient resting period to the used molecule and avoid using all other molecules from the same class.

- Ionophores (all products from a given class) at least six months
- Chemicals at least 12 months (preferably 24 months for products with rapid and very rapid resistance development pace)

# 4.

Consider chemical clean-up and use of vaccines to restore sensitivity toward anticoccidial drugs.

# 5.

Strictly follow the registered dose ranges and follow the established and required withdrawal periods. If there is a dose range registered, consider the infection pressure when choosing the actual dose.

# Know the different product forms





In order to achieve the best performance of an anticoccidial program the molecule should be properly dosed and mixed into the feed, so each and every bird on the farm receives the same adequate amount of the anticoccidial drug.

If some birds are underdosed then they will not be adequately protected, suffer subclinical or even clinical coccidiosis and increase the infection pressure on the farm by an excessive shedding of oocysts. On the other hand, if some birds are overdosed, they might experience side effects - feed refusal, decreased BWG, locomotory or neural disorders like lameness and even increased mortality.

For this reason, proper dosing and mixing, but also a good product form is essential.

Anticoccidial products come in a number of different forms including both granulated products, where the active ingredient is distributed within the granules during the granule production process (such as spray drying, high shear granulation, roll compaction etc.) and simple mixtures of the active ingredient with different carriers. The product form characteristics – particle shape and size distribution, uniformity, durability and content of the active in the fines and dust determines the physical characteristics and, consequently, the performance of the anticoccidial in the feed mill when these products are blended into a premix or feed.

The physical form is important for the quality of the mixture and for the greater or lesser risk of cross contamination between feeds and premix, especially for product of high risk for non-target species (ionophores, nicarbazin, halofuginone).

Granulation reduces the potential for dust and improves the flowability of the product. With less dust this can reduce the amount of fine material remaining on the walls of the equipment and utensils, and therefore, lower the risk of contamination of non-target feeds. (cross contamination).

Phibro carried out an evaluation with the IPT (Institute of Technological Research of the State of São Paulo - Brazil), at the Chemical Process and Particle Technology Laboratory of the Center for Process and Products Technology in 2012, with the objective of determining flowability properties of some anticoccidial products available on the market. Some of the parameters evaluated, as well as the results are listed below and in Table 1.

Angle of repose - it is an indirect measure for which we can estimate the flowability of a product in the premix and feed production lines. The smaller the angle of repose, the lower the piles are formed and the easier it is to flow.

#### **Reference Values:**

25-30° - excellent flowability; 31-35° - good flowability; 36-40° - acceptable flowability; 41-45° - reasonable flowability; 46-55° - poor flowability; 56-65° - very poor flowability; Above 65° - extremely poor flowability (USP, 2006).



#### **Compressibility or Carr Index (CI)**

Simple method to indirectly evaluate the flow properties of powders or formulations by comparing aerated density (pa) and packaged density (pc), with CI calculated by: CI= (pc- pa/ ρc)×100 (USP, 2006).



#### **Carr Index Values (%):**

< 10% excellent flowability; 11 to 15% good flowability; 16 to 20% fair flowability; 21 to 31% poor flowability. 16 to 31% poor flowability (cohesive powders); > 32% very poor flowability.

#### Table 1. Summary of IPT evaluations:

Results of flow properties of combinations of nicarbazin + ionophore

|  | Aviax® Plus<br>(Nicarbazin +<br>Semduramicin) | Combination<br>Nicarbazin<br>+ Ionophore |
|--|---|--|
| Physical Shape                               | Granular                                      | Powder,<br>vegetable<br>carrier          |
| Angle of repose (°)<br>with SD*              | 31,0±1,8°                                     | 43,2±1,8°                                |
| Compressibility or Carr<br>Index (%) with SD | 4,3±0,1                                       | 11,4±0,4                                 |

\*SD – Standard deviation

Comparing the two combinations of nicarbazin + ionophores evaluated, it can be seen that the physical shape is important for the flow characteristics evaluated. The combination of nicarbazin + ionophore in granular form (Aviax<sup>®</sup> Plus) is superior to the association of nicarbazin + ionophore, whose presentation is in the form of a powder with a vegetable carrier.

When selecting an anticoccidial product it is important to select a safe product that has homogenous distribution in the premix and feed and minimizes the risk of carry over to sensitive species feed and withdrawal feed, which can lead to residues in the meat. As already illustrated in the data above, product form can play a crucial role in homogenous distribution, carryover risk and therefore, safety of the product.

In **Table 2** and in the figures are the physical presentations of some anticoccidial products available on the market. The presentations in granulated form favor mixing and reduce the risk of cross contamination, thus decreasing their adherence to the surfaces of equipment in the feed or premix plant.

#### Table 2. Product Forms\*

|   |                          | Aviax <sup>®</sup> Plus<br>Nicarbazin +<br>Semduramicin | Nicarbazin<br>+ Narasin                                  | Nicarbazin +<br>Maduramycin         | Nicarbazin +<br>Monensin | Nicarbazin +<br>Salinomycin  |
|---|--------------------------|---|--|-------------------------------------|--------------------------|--|
|   | Supplier                 | Phibro Animal<br>Health                                 | A  | В                                   | С                        | D  |
| þ | Physical<br>presentation | Granular<br>(2 molecules<br>in the same<br>granule)     | Granular<br>(granules<br>separated for<br>each molecule) | Powder<br>with vegetable<br>carrier | Granular                 | Granular powder<br>Nicarbazin<br>powder and<br>Salinomycin<br>granular |
|   |                          |   |  |                                     |                          |  |





## Nicarbazin + Salinomycin

Nicarbazin powder and granulated salinomycin. Powder-like product..





## Nicarbazin + Narasin

Yellow granules (nicarbazin) and dark granules (narasin).



# G

# Aviax® Plus

Granules contain both active ingredients (semduramicin and nicarbazin).

# Nicarbazin + Monensin

Same granule with nicarbazin and monensin.

# Nicarbazin + Maduramicin

nicarbazin + maduramicin powder mixed with vegetable carrier.

Products in granular presentation are preferable to other physical presentations in terms of safety (less risk of poor homogeneity and overdose or cross-contamination) and provide better mixability for premix ration.



# Know your supplier



A detail often not taken into account in the decisions of anticoccidial programs is the guarantee of supply. It is not uncommon for the companies' purchasing department to close super-special commercial conditions with suppliers who, in the desire to guarantee a good deal, promise volumes they cannot supply. Many of these suppliers have their final products and active ingredients imported, which can generate a certain complexity in supply chain management and non-compliance with commercial agreements.

At that moment, all the effort to choose an anticoccidial program can go down the drain, since the lack of product compromises the entire operation and, consequently, the performance results. Not to mention the wear and tear generated by the need to seek a new supplier at the last minute to meet the demanded volumes.

When choosing anticoccidial programs and other additives, it is recommended to look for manufacturers that can meet the volumes requested for the necessary period and that have robust local logistics, which avoid this type of risk of lack of supply.

# Know the supplier's know-how regarding services and other differentials

programs.

It is obvious that special commercial conditions are always attractive, but the quality and knowhow of the supplier must have an important weight in the decision.

An anticoccidial program goes beyond the choice of an active ingredient to be used. There is a whole job of education and training of professionals who deal with birds on a daily basis to learn about the problems, make a more accurate diagnosis, ensure the implementation of rules and procedures that avoid risks of cross contamination, presence of residues and application of best practices in the management of the coccidiosis theme.

For this reason, the choice of the supplier should go beyond a purely commercial view, that is, the one with the best price, but the one that can add value to the production process, in risk management and in the training of company professionals.

Perhaps this is one of the most important topics to be considered when deciding on anticoccidial

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